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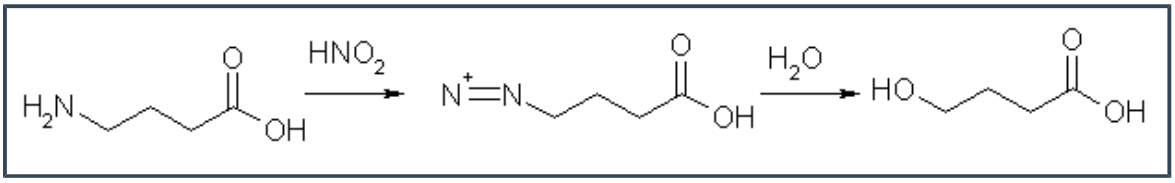
SANDMEYER REACTION OF GABA TO GBL/GHB

by Chromic

QUICK INTRODUCTION

As other writeups that I have published, this method is 100% OTC. It is awesome for a chemist who wishes to prepare GHB in small quantities and high yields and to do so without directly obtaining any regulated chemicals such as gamma-butyrolactone (GBL) or 1,4-butanediol (BDO). It also avoids the typically low yields seen from the oxidation of tetrahydrofuran (THF). It uses an easy to obtain amino acid, gamma-aminobutyric acid (GABA), and sodium nitrite ($NaNO_2$). It scales very nicely and runs without too much hassle. Not one suspect chemical is used.



The Sandmeyer reaction uses nitrous acid to turn amines into diazonium salts. This reaction, as it applies to turning GABA into GHB, is shown in the first reaction below. Aliphatic diazonium salts rapidly undergo hydrolysis in the presence of water giving off nitrogen gas and leaving a hydroxyl group behind. This is shown in the second step. As a result of these reactions, GABA can be turned into GHB in an easy to perform one-pot reaction.

RUNNING THE REACTION

Set up a 2L flask, sitting in ice-water on top of a magnetic stirrer. Now:

1. Add 3mol GABA (309.4g)
2. Add 3mol $NaNO_2$ (207.0g)
3. Add 700ml water (total volume becomes about 1100ml)
4. Drop in a 1" stir bar and start stirring
5. Charge a 500ml pressure equalized addition funnel with 3.3mol HCl(aq) (385.0g 31.25%, 334.8ml 31.25%)
6. Fit the addition funnel with a gas outlet adapter and vent to theoutside

Begin slowly dripping the hydrochloric acid into the mixture. Drip it in at a constant rate of about 1 drop every 2-5 seconds. Speed it up as time progresses and replace the ice as necessary, but do not allow the evolution of the brown poisonous gas to become vigorous. After about one hour after the last drop of acid has been added, there is no need to replace the ice. Once the reaction is done, proceed to extract. (usually 24-36 hours later)

EXTRACTING THE GOODS

There are many options for this. This is still a work in progress, but after about 20 runs, I came to use this work up. You can use ethyl acetate (EtOAc), chloroform or methylene chloride (dichloromethane aka DCM) to perform the solvent extractions. I have normally used DCM as it's nice since the organic layer drops to the bottom of the separatory funnel.

1. Setup for a simple distillation.
   a. Distill, throwing out the first 5-10mls, or so, of distillate as it will contain a fair amount of nitric oxides. Distill off as much water as possible, basically until the sodium chloride starts to saturate the aqueous layer and precipitate out.

b. The remainder of the distillate (approximately 700ml) will contain approximately 1g GBL/10ml.
c. Treat the remainder of the distillate with $NaHCO_3$ at reflux for 30 mins
d. Boil with about a 5% volume of activated charcoal (ie 35ml activated charcoal) (compared to the volume of the solution) for 5-10mins.
e. Allow it to cool and filter, wash the charcoal with distilled water. Save the NaGHB.

2. With the remainder of the aqueous, extract 5 times with 625ml portions of DCM.
3. Distill off the DCM (reuse that DCM!).
4. Distill the GBL (under vacuum if available).
5. React with $NaHCO_3$ and distilled water and treat with activated charcoal as before.

Typically 375g of NaGHB is made from the solvent extracted GBL and 100g NaGHB from the aqueous distillate. Although conversion is nearly quantitative (as measured by GC/MS), the overall recovered yield is usually about 70%.

For those who don't know how to make NaGHB from GBL using $NaHCO_3$ please read the section on preparation of Sodium GHB using Sodium Bicarbonate (Baking Soda, $NaHCO_3$) found in the GHB faq. Never use unknown grades of NaOH--they may contain toxic heavy metal contaminants.

OTC chemicals rock. The war is over.

NOTES ON PROCEDURE

- 1M $NaNO_2$/GABA, as the French ref states is far, far too much water. You don't need it. I don't use that much.
- It's possible to reduce the water further, down to the minimum necessary to dissolve the NaCl formed, thus avoiding the distillation of the aqueous layer. The trouble with this is that it's not fully practical. All of the GABA/$NaNO_2$ will not dissolve, and you'll see more of an evolution of nitric oxides. The amount of water used is just barely enough to dissolve all of the $NaNO_2$ and GABA to begin with.
- If you want to skip the simple distillation (steps 1a-e) and go straight to step 2 (the extraction with the organic solvent) make sure to increase your organic solvent amounts by about 20%. Your yields will go down slightly.
- It's possible to used sulfuric acid, however Na_2SO_4 is not as soluble as NaCl is, mole for mole. You'll need to use more water.
- It's possible to use just a little bit less HCl, but hey, a slight excess is always a good idea.
- It's possible to dump in a fair amount more HCl to try and push the GBL into the organic layer. It doesn't really work that well though. Yields don't go up.
- It's possible to use chloroform or ethyl acetate instead of dcm. Diethyl ether will work as well. Do not try to use anything more nonpolar such as toluene, hexanes or the like. They won't extract much GBL.
- Figuring out where the other 30%+ of the yield is going has been frustrating. Perhaps it is staying in the aqueous as free GHB. But do not consume the post-reaction aqueous layer!
- The GBL produced from distillation has an putrid sour smell. This is likely trace quantities of butyric acid (the molecule responsible for the smell of rancid butter). It is not toxic in trace quantities and the off-smell and off-taste is cleared by treatment with activated charcoal.
- The dose/response curve for NaGHB is exponential. 2g may be a nice buzz, 2.5g an amazing high, and at 3g a novice user could be violently ill, passed out and completely unresponsive. These doses are guidelines. Every person's response will vary. Chronic use of GHB will result in tolerance and physical addiction. Never mix with any other CNS depressants (especially alcohol).

REFERENCES

1. **Bull. Soc. Chim. Fr.; 1; 88-94 (1989)**

2. **GHB Letter to the Alabama Senate Committee on the Judiciary**

ACKNOWLEDGEMENTS

Last, but surely not least, come the thank yous!

First, thank you to the girl who will always have a special place in my heart (and your determination in helping me with my struggles, especially my addiction to GHB and alcohol).

Thank you Rhodium for your hard-work and dedication to your site and the Hive in general. Thank you for pushing me to publish this document. A big round of applause for Steven Fowkes (even though you got your info wrong on MSG -> GBL in one step rxn), Fierceness, Moo, StraightEdge, hCiLdOdUeDn, Roundbottom, Osmium, Bright Star, Methyl Man, Dr_Sister, AB2, Aztec, Hypo, Ueruma, Ezekill, Terbium, Antoncho, Eleusis and Sasha Shulgin for raising my knowledge, awareness and inspiration. :)

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